

The Need for Inhalation Reference Concentration Values for Acute and Other "Less-than-lifetime" Exposure Durations

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ABSTRACT

EPA has historically developed reference concentration (RfC) values for non-cancer health effects based solely on a chronic exposure scenario (e.g., continuous exposure: 24 hours/day, 7 days/week for a 70-year lifespan). Emissions of toxic air pollutants, however, do not always result in such a consistent exposure pattern. The need has intensified during the last few decades within the risk assessment community to address health effects from higher levels of exposure to toxic air pollutants that would occur for shorter durations of exposure. This need has increased with the realization by many regulators within the EPA of the relevancy of acute (single exposure, less than or equal to 24 hours) and other less-than-lifetime exposure scenarios to the Agency's mission (i.e., to protect human health and the environment). A variety of occupational guidelines for acute exposures currently exist; however, the intent of these values (e.g., National Institute of Occupational Safety and Health permissible exposure levels [PELs], ACGIH threshold limit values [TLVs]) addresses responses that may be specific to a worker population, include considerations in addition to health effects (e.g., monitoring feasibility), and may not necessarily be regarded as safe for the general population. The emergency response guidelines for acute exposures (e.g., Acute Exposure Guideline Levels [AELs] and Emergency Response Planning Guidelines [ERPGs]) are designed for very specific scenarios ("once-in-a-lifetime" types of events) with an assumption of only one exposure event. They are not applicable when short-term, "higher-than-average" exposures occur on a more routine basis nor do they consider exposure to residual levels of contaminants in the periods following a catastrophic release. These considerations are important, however, when making decisions regarding exposures following an event such as the aftermath of Hurricane Katrina or for clean-up and re-occupancy following an event involving Homeland Security. The combination of demand for and lack of appropriate short-term reference values for these scenarios have made this need critical. Acute RfCs are being developed by the National Center for Environmental Assessment (NCEA) as a first step in addressing a number of these concerns and to provide some of the values needed to accomplish the Agency's mission. Presented here are descriptions of the various scenarios within the Agency to which acute RfCs would be available, as well as a comparison and contrast of the acute RfCs with other available acute guidelines. A current timeline and status of methods development for acute RfCs is also provided.

[The views expressed in this poster are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.]

Agency Needs

Both Development of a Methodology to derive Acute and < Lifetime RfCs and the RfC values themselves will support several EPA Programs and Activities.

Program and Regional Offices

Regulatory Analysis

- **OAR / OAQPS** – "Residual Risk" and "Community Assessment" Programs
- **OAR / OTAQ** – "Near Roadway" and "In Vehicle" environments
- **OAR / Indoor Air** – Acute effects cause most complaints and lost productivity

Regulatory Support

- **Superfund** – Risk Assessment Guidelines (RAGs) ask for Acute and Chronic Assessments
- **Regions** – Interpretation and evaluation of monitoring data (typically 1-8 hr)

Homeland Security

Acute Exposure Guideline Levels – AELs (OPPTS / OPPT)

- Designed for use in Emergency Response
- Accidental or Intentional Releases

Provisional Advisory Levels – PALs (ORD / NHRSC)

- Designed for longer durations than AELs
- Needed for all exposure durations (see Figure below)

Safe Levels for Re-occupancy (White House / OSTP / Multi-Agency Subcommittee)

- Potentially repeated exposure
- Persistence of chemical agent or toxin
- Evaluating Risks from indoor air exposures

Categories of Acute Health Reference Values

(Table from Woodall, 2005)

Occupational

- Healthy worker population
- Exposures for average work day/week and short-term peaks
- Consideration of factors other than health risk

Emergency Response

- General population – not necessarily the "most susceptible"
- Rare, short-term exposures (e.g., once-in-a-lifetime)

General Public Health Protection

- All susceptible individuals (generally more conservative)
- More routine, potentially repeated exposures

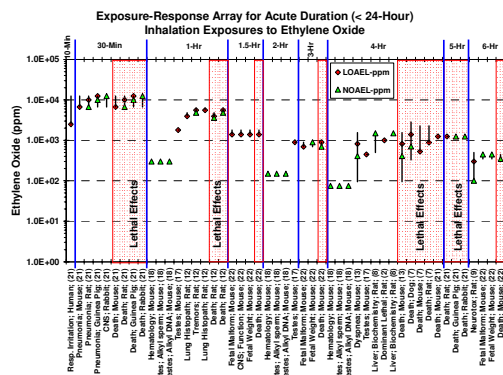
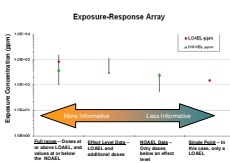
Reference Value	Organization	Exposure Duration
PEL - Permissible Exposure Limit	OSHA	8-hour - Time Weighted Average (TWA)
Ceiling	OSHA	Up to 10-minute
REL - Recommended Exposure Limit	NIOSH	8-hour TWA
IDLH - Immediately Dangerous to Life and Health	NIOSH	Up to 30-minute
STEL - Short Term Exposure Limit	NIOSH	15-minute
TLV - Threshold Limit Value	ACGIH	8-hour TWA
TLV-STEL - TLV Short Term Exposure Limit	ACGIH	15-minute
AEGL - Acute Exposure Guideline Level	NAC/AEGL; NRC/AEGL	10- and 30-minute; 1-, 4- and 8-hour
ERPG - Emergency Response Planning Guideline	AIHA	1-hour
TEEL - Temporary Emergency Exposure Level	DOE	1-hour
ERG - Emergency Response Guidebook	DOT	Specialized application
MRL - Minimal Risk Level	ATSDR	1-14 days (acute); 15-364 days (intermediate); >365 days (chronic)
CA-REL - Reference Exposure Level	Cal-EPA OEHHA	1-8 hours
EPA - Acute RfC	US EPA / IRIS	1-, 4-, 8-, and 24-hours

Comparisons between EPA Inhalation Health Reference Values

Severity		Duration Categories (RID/RfC Improvement Document Definition – US EPA 2002)				
		Acute ($< 24\text{-h}$)		Short-Term (1-30 days)		Long-Term (30-d to 7-yr)
Lethal	AEGL-3	24-Hour PAL-3	30-Day PAL-3	2-Year PAL-3		
Disabling/ Irreversible	AEGL-2	24-Hour PAL-2	30-Day PAL-2	2-Year PAL-2		
Irritation / Mild Asymptomatic	AEGL-1	24-Hour PAL-1	30-Day PAL-1	2-Year PAL-1		
No Adverse Effects “Presumptively Safe”	Acute RfC		ATSDR Acute-MRL	ATSDR Intermediate-MRL	ATSDR Chronic-MRL	Chronic RfC
			Short-Term RfC		Subchronic RfC	
		8-h	24-h	30-d	7-yr	70-yr
Duration of Exposure						

Innovations

The **Exposure-Response Array** allows a Risk Assessor to view the relationship between duration and concentration of exposure in one view across multiple studies, species, and endpoints. The figure to the right provides a guide to how data are displayed. The figure below is the example of the Exposure-Response Array for acute Ethylene Oxide exposures (Note: the numbers in the lower x-axis are a key to study references).



Progress and Path Ahead

Example Acute Assessments

- Ethylene Oxide
- Hydrogen Sulfide
- Hexachlorocyclopentadiene
- Phosgene

Synthesis Document

- Preliminary Methodology Documentation
- Based on previous documents (US EPA 2000, 2004)
- Incorporates "lessons learned" from Example Acute Assessments

Exposure-Response Database

- Serves as a centralized "shared resource" – being used by NHRSC in PAL development and OPPT in AEGL development.
- Source of data for development of Exposure-Response Arrays
- First step toward a more globally available resource (Woodall, 2004)

Reviews – Applied to all Documents

- Standard IRIS Agency Review
- OMB Review
- Science Advisory Board (SAB) as the Final External Peer Review

Supplemental Documents

- **Additional Assessments**
 - Chemical classes not addressed (e.g., metals and organo-metals)
 - Seeking Program Office Input on candidates
- **Additional Issues**
 - Reset times – how long between acute exposures is needed to return to a "base state" where a similar exposure may be tolerated.
 - Development of duration-appropriate dosimetry metrics – "beyond" C₁ × T and Haber's rule.
- **Additional Tools and Guidance on Existing Tools**
 - Dosimetry Study to inform going "beyond" C₁ × T and Haber's rule
 - Refinement in approaches to using Benchmark Dose Software (BMDS) and the Categorical Regression (CatReg) approach.

Final Acute and < Lifetime Inhalation Assessment Method

- Being developed in concert with revisions to Chronic RfC Method
- Expected completion in FY 2008

References

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